REMARKS/ARGUMENTS

In response to the Office Action of July 28, 2005, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Claim Status/Support for Amendments

Claims 1, 39, 40 and 44 have been amended. Claims 2-38 were cancelled in a previous response (filed on June 9, 2003). Claims 39-46 are withdrawn from consideration. It is understood that claims 39-46, drawn to the non-elected invention, will remain pending, albeit withdrawn from consideration on the merits at this time. If the examined claim of the Group I invention is deemed to be allowable, rejoinder of the remaining claims (39-46) in accordance with the decision in *In re Ochiai* is respectfully requested; since the remaining claims (39-46) are limited to the use of the biopolymer marker of claim 1 (the examined claim of the elected Group I invention).

Claim 1 is currently under examination. Claims 1 and 39-46 remain pending in the instant application.

No new matter has been added by the amendments to the claims made herein.

Claim 1 has been amended to clearly indicate that the

biopolymer marker consisting of amino acid residues 2-18 of SEQ ID NO:1 evidences a link to Alzheimer's disease. This amendment is supported by the specification as originally filed; page 35, lines 14-18, disclose that an objective of the invention is to evaluate samples containing a plurality of biopolymers for the presence of disease specific biopolymer markers which evidence a link to at least one specific disease state and page 46, lines 11-19 identify SEQ ID NO:1 as a biopolymer related to the specific disease, Alzheimer's disease.

Claims 39 and 44 have been amended to remove the term "isolated".

Claim 40 has been amended to provide proper antecedent basis to the term "sample" in parent claim 39.

Request for Rejoining of Claims

Considering that claims 39-46 are limited to the use of SEQ ID NO:1 a search of these claims would encompass this specific sequence. The instant application is related in claim format to several other applications, both pending and issued, of which serial number 09/846,352 is exemplary. In an effort to maintain equivalent scope in all of these applications, Applicants respectfully request that the Examiner consider rejoining claims 39-46 in the instant application, which are currently drawn to non-

elected Groups, with claim 1 of the elected Group under the decision in *In re Ochiai* (MPEP 2116.01), upon the Examiner's determination that claim 1 of the elected invention is allowable and in light of the overlapping search. If the biopolymer marker of SEQ ID NO:1 is found to be novel, methods and kits limited to its use should also be found novel.

Amendment Compliance with 37 CFR 1.121

The Examiner has indicated that the amendment to the claims filed on April 4, 2005 is considered non-compliant because it has allegedly failed to meet the requirements of 37 CFR 1.121, as amended on June 30, 2003, with respect to the status of claims 39-46. Because claims 39-46 are withdrawn from consideration, the correct status of these claims is "withdrawn". The Examiner has required appropriate correction.

Applicants respectfully submit that the Examiner is incorrect. The correct status of a withdrawn claim which is currently amended is "withdrawn-currently amended"; see MPEP Appendix R, Patent Rules, 37 CFR 1.121 c (1)(ii).

Withdrawn claims 39, 40 and 44 amended herein are indicated as such in compliance with 37 CFR 1.121.

Declaration under 37 CFR 1.132

Applicants herein provide the attached Declaration (and figure) under 37 CFR 1.132 in order to more clearly disclose the gel from which the claimed biopolymer marker was obtained (amino acid residues 2-18 of SEQ ID NO:1). The figure attached to the declaration was produced by scanning the original photograph of the gel. No new matter has been added; this figure is simply a clearer copy of Figure 1 as originally filed is provided to clarify the presence and/or the absence of the bands. The figure entitled "DEAE 3 (Elution) AD vs. Age Matched AD (Control)" represents Figure 1.

The gel shown in the figure attached to the declaration does not represent new experimentation; the figure shows a clearer image of the original gel made at the time that the experiments described in the instant specification were first carried out.

Rejection under 35 USC 101

Claim 1, as presented on April 4, 2005, stands rejected under 35 USC 101 because the claimed invention allegedly has no apparent or disclosed specific and substantial credible utility.

Applicants respectfully disagree with the Examiner's contention and assert that the claimed invention has both a specific and a substantial credible utility.

The Examiner asserts that the instant specification describes

the finding of a specific fragment of apolipoprotein J precursor protein (amino acid resides 2-18 of SEQ ID NO:1) in serum samples from patients diagnosed with Alzheimer's disease.

Applicants respectfully contend that this statement reveals the Examiner's incomplete understanding of the invention. Increased expression of the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) is found in patients age-matched with the Alzheimer's patients and **not** in Alzheimer's patients. This phenomenon can be observed in the figures as originally filed and is explained at various points in the previous response filed on April 4, 2005 (see, for example, pages 22-24). Additionally, the instant specification as originally filed clearly indicates that the criteria for labeling a peptide a "marker" is differential expression in disease vs. normal, i.e. the definition of "marker" according to the invention is not limited to peptides found in a disease state and absent in a normal state (for example, see page 5, lines 12-20).

The Examiner makes several assertions regarding the term "biopolymer marker". The Examiner asserts that there is no explanation presented at the time of filing as to what constitutes a "biopolymer marker". Is it the presence/absence of the claimed peptide (amino acid residues 2-18 of SEQ ID NO:1) that is indicative of a disease? Or the up or down regulation of the marker

relative to categorization of disease state? The Examiner further asserts that it appears in order to practice the claimed invention a skilled practitioner would have to engage in significant further research to determine if a peptide of amino acid residues 2-18 of SEQ ID NO:1 is absent or present or present strongly in all or any tissue samples of a person suspected of having Alzheimer's disease, or is up-or down-regulated in disease in order to establish if the claimed peptide could be used as a marker for Alzheimer's disease.

Applicants respectfully submit that the Examiner's statements reveal an incomplete understanding of the claimed invention. Additionally, the Examiner appears confused regarding the meaning of the term "biopolymer marker".

A careful review of the instant specification shows that the term "biopolymer marker" is explicitly defined at page 21, line 20 to page 22. Thus, contrary to the Examiner's assertion, there was an explanation of the term presented at the time of filing. Additionally, the instant specification discloses several times how a peptide is identified as a biopolymer marker, see for example, page 5, lines 12-20 and page 11, lines 9-20. The instant inventors isolated the claimed peptide (amino acid residues 2-18 of SEQ ID NO:1) by carrying out the disclosed protocols (chromatography and mass spectrometry), noted the expression in age-matched patients relative to expression in Alzheimer's disease patients, subjected

the noted expression pattern to the criteria as presented on page 11, lines 9-20, and, thus identified it as a biopolymer marker for Alzheimer's disease. The mass spectral profile established for the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) is presented in Figure 2 and is intended to be used as a reference for evaluation of unknown samples. Accordingly, contrary to the Examiner's assertion, a skilled practitioner would not be required to engage in significant further research to establish if the claimed peptide can be used as a marker for Alzheimer's disease since the specification discloses the mass spectral profile of the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) as a diagnostic tool. The information presented in the instant specification, such as that on page 5, lines 12-20 and page 11, lines 9-20, is presented to indicate how the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) was evaluated and is meant to teach one of ordinary skill in the art how to duplicate the findings of the instant inventors.

The Examiner uses two hypothetical examples which allegedly support her position. The first is a hypothetical specification which claims a peptide that is expressed in colon cancer and not expressed in healthy colon tissue. This hypothetical specification does not disclose the biological activity of the claimed peptide. The Examiner asserts that the claimed peptide in this hypothetical

example has utility and is enabled as a colon cancer marker. Alternatively, the Examiner also suggests a hypothetical example in which a claimed peptide is expressed at specific altered levels in colon cancer as compared to healthy colon tissue. The Examiner asserts that one skilled in the art would immediately recognize that the claimed peptide in this hypothetical example would be useful as a colon cancer marker. However, the Examiner insists that the instant situation does not follow the fact pattern in either hypothetical example.

The instant specification discloses that the claimed peptide (amino acid residues 2-18 of SEQ ID NO:1) is expressed at increased levels, i.e. altered levels, in age-matched patients as compared to Alzheimer's disease patients. Thus, applying the reasoning of the Examiner, one skilled in the art would immediately recognize that the claimed peptide in the instant specification would be useful as a marker for Alzheimer's disease. Accordingly, contrary to the Examiner's assertions, the instant situation does follow the same fact pattern as the Examiner's hypothetical examples.

The Examiner asserts that if the claimed peptide is not diagnostic for any pathological condition, including Alzheimer's disease, then it is not obvious why it is termed as a marker.

Applicants respectfully disagree with the Examiner's assertion.

The claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1), although not specifically diagnostic of any condition, is present at altered levels in tissue samples from Alzheimer's disease patients and patients age-matched to the Alzheimer's disease patients. It is acceptable in the art to refer to a differentially expressed peptide as a "marker". For example, Cheng et al. (see attached abstract, Journal of Neural Transmission 103 (4):433-446 1996; reference 1) identify homovanillic acid as a useful marker for early diagnosis of Parkinson's disease since when comparing the levels of homovanillic acid in cerebrospinal fluid, they found a lower level in Parkinson's disease patients as compared with the levels found in age-matched controls.

Thus, Applicants respectfully submit that, contrary to the Examiner's assertion, it is obvious why a worker of ordinary skill in the art would refer to the claimed peptide (amino acid residues 2-18 of SEQ ID NO:1) as a marker for Alzheimer's disease.

Additionally, the Examiner continues to maintain the assertion that the instant application does not disclose a specific biological role for the claimed peptide, or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

In order to satisfy the requirements of 35 USC 101, an applicant must show that the claimed invention is "useful" for some

purpose either explicitly or implicitly (see MPEP 2107.01).

Claim 1 is drawn to a biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) which is disclosed as predictive of and/or related to Alzheimer's disease in the specification as originally filed (page 46 and original claims 1 and 2). Figure 1 evidences the increased presence of the claimed biopolymer marker in patients who were age matched with Alzheimer's disease patients. Clearly, the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) represents a diagnostic tool for Alzheimer's disease. Applicants respectfully submit that the showing of "differential expression" of the claimed biopolymer marker is sufficient to establish the credibility of the stated utility for the claimed biopolymer marker, i.e, no specific biological role for the peptide or information of how to manipulate for a desired clinical effect is required. Thus, Applicants explicitly show that the claimed biopolymer marker is useful.

However, the Examiner apparently does not find this use credible.

It has been established that where an applicant has specifically asserted that an invention has a particular utility, the assertion cannot be simply dismissed by Office personnel as being "wrong", even when there may be a reason to believe that the assertion is not entirely accurate (see MPEP 2107.02 III B).

Claim 1 has been amended to recite that the isolated biopolymer marker consisting of amino acid residues 2-18 of SEQ ID NO:1 evidences a link to Alzheimer's disease.

At page 46, the instant specification as originally filed, discloses that SEQ ID NO:1 is a fragment of apolipoprotein J precursor protein.

An objective of the instant invention is to evaluate samples containing a plurality of biopolymer markers for the presence of disease-specific markers which evidence a link to a specific disease state (see the instant specification as originally filed at page 35, lines 14-18). According to the web site dictionary.com the term "linked" refers to the condition of being associated with or connected to (see attached document as accessed from the internet; reference 2). Applicants respectfully assert that the instant specification fully supports a connection and/or an association of the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) with Alzheimer's disease. The claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) was identified as related to Alzheimer's disease by carrying out the protocols disclosed in the specification (see page 46,lines 11-19 of the instant specification as originally filed). The data presented in Figure 1 clearly evidences that the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) was found to be

differentially expressed between Alzheimer's disease patients and patients age-matched with the Alzheimer's disease patients. Thus, Applicants assert that the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) is useful for diagnosis and treatment of Alzheimer's disease (an "asserted" utility).

Accordingly, Applicants respectfully submit that it is improper for the Examiner to simply dismiss the evidence as presented by the instant specification (and discussed above) and continue to maintain the assertions that the instant application provides no utility for the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1).

Furthermore, the Examiner is reminded that an Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement under 35 USC 101 (see MPEP 2107.02 III A). Thus, the requirements of 35 USC 101 are met solely by Applicants' above assertion regarding the use of the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1).

Applicants' statement of an asserted utility also constitutes a specific and substantial utility that is supported by the specification as originally filed (see page 1, lines 5-13, page 35, lines 14-18, page 46, lines 11-19 and Figures 1 and 2).

The claimed biopolymer marker (amino acid residues 2-18 of SEQ

ID NO:1) does not evidence a link to a myriad of unspecified diseases but rather evidences a link to a specific disease, Alzheimer's disease, thus the invention has a "specific" utility.

The Examiner asserts that the instant specification fails to explain the relationship between a peptide 2-18 of SEQ ID NO:1 and "particular disease state".

Applicants respectfully disagree with the Examiner's assertion.

The instant specification, as originally filed, is very clear that it is the differential expression of a peptide between two different physiological states, for example, a particular disease state and a normal state, which determines the relationship of a peptide to a disease state (see, for example, page 1, lines 5-13 and page 5, lines 12-20).

The differential expression of the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) between Alzheimer's disease and a "normal" (patients age-matched with the Alzheimer's disease patients and "normal" with regard to Alzheimer's disease) physiological state links the biopolymer marker to Alzheimer's disease.

Apparently, the Examiner believes that differential expression is an insignificant characteristic to consider when evaluating a peptide as a potential marker. Applicants respectfully disagree

with the Examiner's view.

In the search for specific biomarkers, proteins found to be differentially expressed between "disease" and "normal", are frequently identified as potential targets for diagnostics and/or therapeutics.

For example, Scott D. Patterson presents the state of the art in mass spectrometry/proteomics by summarizing the Asilomar Conference on Mass Spectrometry (see attached article, Physiological Genomics 2:59-65 2000; reference 3). This conference took place in 2000, thus coinciding with the time that the instant inventors were working to develop the instant invention.

In the disclosed method of the instant invention, proteins (as seen on a gel) that are identified as differentially expressed between a disease and a non-disease state are selected for excision (from the gel) and identification (see, for example, page 38, lines 14-18 of the instant specification as originally filed, and Figure 1). Such selection methods are common practice in the search for biomarkers of specific physiological states. For example, at page 61, right column of Patterson, several automation processes are discussed in the section titled "Automated identification of gel-separated proteins by mass spectrometry". This discussion begins with the following statement:

"Following quantitative analysis of 2-DE patterns, the next

step is the identification of all protein spots that display differential expression."

Thus, it is concluded that it is known practice to select potential disease markers by their differential expression between a disease and a non-disease state.

Furthermore, Applicants respectfully submit that many of the methods disclosed in the instant specification are routinely practiced by those of ordinary skill in the art attempting to identify biomarkers of particular physiological states. For example, at page 64, left column of Patterson is a description of the SELDI approach (as discussed at the conference by Scot Weinberger) wherein defined chemical/biochemical surfaces are utilized to allow fractionation of proteins from biological fluids in a reproducible manner. This reproducibility allows comparisons between different samples to be made. Weinberger described a search for markers of benign prostate hyperplasia that, like prostate cancer, displays elevated prostate specific antigen (PSA) levels. The fraction exhibiting a difference between these samples was able to be enzymatically digested, and a number of peptides were generated. These peptides were able to be fragmented using the MALDI-Qq-TOF(a procedure described by Ken Standing at the conference, page 62, left column of Patterson). It was found that there appears to be a difference in the relative level of

seminogelin fragments between these two states (prostate cancer and benign prostatic hyperplasia), thus providing a potential differential marker.

Applicants respectfully draw the Examiner's attention to the fact that the method described by Weinberger is analogous to the method described in the instant specification. Furthermore, when interpreting data Weinberger uses the same approach to interpretation as the instant inventors in order to identify seminogelin fragments as a potential marker to distinguish between benign prostate hyperplasia and prostate cancer based on differential expression of the fragments. Additionally, Applicants respectfully point out to the Examiner that Weinberger linked differential expression of seminogelin to benign prostate hyperplasia and prostate cancer without analysis of a sample from a control patient free of disease or analysis of a sample from a patient having another disease, which is not benign prostate hyperplasia or prostate cancer. Such linking of markers with disease through differential expression is commonly practiced in proteomics.

Furthermore, it has been settled that an applicant is not required to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt". Instead, evidence will be sufficient if, considered as a whole, it leads a

person of ordinary skill in the art to conclude that the asserted utility is more likely than not true (MPEP 2164.07 I C).

Figure 1 establishes that the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) is differentially expressed between Alzheimer's disease patients and patients age-matched with the Alzheimer's disease patients. As pointed out above, one of skill in the art would recognize differentially expressed peptides to be potential markers for a disease condition. Thus, differential expression of a peptide between a disease state and a normal state is enough information to label a peptide a "marker" for the disease condition, no additional validation or further research is necessary.

Accordingly, Applicants respectfully contend that one of skill in the art would believe, based upon the information in the specification in light of the knowledge in the prior art, that the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) is more likely than not to be a marker of Alzheimer's disease.

The Examiner asserts that the specification does not disclose a credible "real-world" use for the claimed biopolymer marker and contends that the instant situation is directly analogous to that which was addressed in *Brenner v. Manson* (148 USPQ 689).

Applicants do not agree with the Examiner's interpretation of the situation addressed in *Brenner* and respectfully submit that it

is not directly analogous to that of the instant situation.

The situation in *Brenner* involved "product by chemical process" claims in which the utility of the process was questioned because the compound produced by the process allegedly had no evidenced utility other than the fact that a homologue of the compound produced was found to have tumor-inhibiting effects in mice. The biopolymer marker of the instant invention (amino acid residues 2-18 of SEQ ID NO:1) is linked to Alzheimer's disease as evidenced in Figure 1, and thus, has utility, in and of itself, as a marker for diagnostics and/or therapeutics of Alzheimer's disease.

Accordingly, Applicants respectfully submit that the facts of *Brenner* are not directly applicable to the facts in the instant situation.

Applicants respectfully contend that the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) has a "real-world" use.

When considering practical utility ("real-world" utility) relevant evidence is judged as a whole for its persuasiveness in linking observed properties to suggested uses (*Nelson v. Bowler and Crossley* 206 USPQ 881).

The instant specification suggests that the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1)is useful for

diagnostics and/or therapeutics of Alzheimer's disease since it was found to be differentially expressed in Alzheimer's disease versus a normal physiological state (patients were age-matched to the Alzheimer's disease patients and are "normal" with regard to Alzheimer's disease). Applicants respectfully submit that the observed differential expression is enough evidence such that one of ordinary skill in the art would be reasonably certain of the practical utility of the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1).

Situations similar to the situation in the instant case have occurred in the prior art wherein a marker was recognized to have practical utility based upon its appearance in a disease state.

For example, Tockman et al. (Cancer Research Supplement 52:2711s-2718s 1992; reference 4) link several biopolymer markers to lung cancer in a manner analogous to the linking of the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) to Alzheimer's disease as disclosed in the instant specification. Tockman et al. state at page 2712s, left column:

"A functional membrane-associated bombesin receptor recently has been isolated from human small lung cell carcinoma (NCI-H345) cells, (23), and bombesin-like peptides have been found in the bronchial lavage fluid of asymptomatic cigarette smokers (24). Thus markers of growth factor expression, insofar as they reflect

oncogene activation, may also hold promise for the detection of early (preneoplastic) lung cancer".

From this statement, it is clearly evident that Tockman et al. link bombesin with small lung cell cancer and recognize its utility with regard to potential diagnostics for small cell lung cancer. It does not appear that bombesin was "validated" or subjected to "further research" prior to this association.

Additionally, Tockman et al. state at page 2713s, left column:

"Evidence of a transformed genome, by expression of tumor-associated antigens, oncofetal growth factors, or specific chromosomal deletions has clear biological plausibility as a marker of preclinical lung cancer".

From this statement, it appears that Tockman et al. believe that the expression of certain proteins provides evidence of a transformed genome and since this transformed genome is associated with lung cancer, it is reasonable to believe that these certain proteins are potential markers. Thus, Tockman et al. employ reasoning similar to that of the instant inventors.

Furthermore, if an invention is determined to have "real-world" value, one skilled in the art can use the claimed discovery in a manner that provides some immediate benefit to the public (as established in *Nelson v. Bowler and Crossley* 206 USPQ 881).

The risk for developing Alzheimer's disease increases with

age. People are living longer and thus, advances in the diagnosis and treatment of Alzheimer's disease would greatly benefit the elderly population by delaying symptoms and improving the quality of life for these people. The claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) is identified as a marker for Alzheimer's disease and thus, represents an advance in Alzheimer's research; a "real-world" use to benefit the public (i.e. the elderly population), which satisfies the precedent set in *Nelson*. Thus, contrary to the Examiner's assertion, the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) has a substantial utility based upon a "real-world" use.

Additionally, the Examiner must provide reasoning and/or evidence to show that one of ordinary skill in the art would doubt the asserted utility of the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) as a marker of Alzheimer's disease (see *In re Brana* 134 USPQ 2d 1436 and MPEP 2107.01 III).

The claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) is identified as a fragment of the apolipoprotein J precursor protein at page 46 of the instant specification as originally filed. Figure 1, both as originally filed and as attached to the declaration filed herewith, demonstrates that the claimed biopolymer marker exhibits greater expression in age-matched control patients than in Alzheimer's disease patients.

Although the prior art does not specifically recognize that the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1), a fragment of apolipoprotein J precursor protein, is related to Alzheimer's disease, a neuroprotective role has been suggested for apolipoprotein J (see reference #8 of the previous response filed on April 4, 2005). Additionally, it has also been suggested that in Alzheimer's disease low cellular expression of this protein may be associated with neuronal degeneration and death (see reference #8 of the previous response filed on April 4, 2005). Applicants' findings that decreased expression of the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) is found in Alzheimer's disease patients is in agreement with prior art data. Thus, Applicants contend that one of ordinary skill in the art would not have any reason to doubt the asserted utility for the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) as a marker predictive for Alzheimer's disease.

Accordingly, Applicants respectfully submit that the Examiner has not met the burden by providing reasoning and/or evidence to show that one of ordinary skill in the art would doubt the asserted utility of the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) as a marker of Alzheimer's disease.

Apparently, the Examiner is requiring Applicants to provide evidence that the claimed biopolymer marker is conclusively a

specific marker for Alzheimer's disease.

The Examiner is reminded that the stage at which an invention in this field (in this case, diagnostics and/or therapeutics for Alzheimer's disease) becomes useful is well before it is ready to be administered to humans. Usefulness in patent law necessarily includes the expectation of further research and development (see *In re Brana* 134 USPQ 2d 1436 and MPEP 2107.01 III).

Thus, Applicants respectfully submit that by requiring evidence that the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) is conclusively a specific marker for Alzheimer's disease is requiring the Applicants to meet a standard higher than that which is necessary to satisfy the utility requirement.

In conclusion, based upon all of the above arguments, Applicants respectfully submit that one of ordinary skill in the art would immediately appreciate why Applicants regard the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) as useful.

Accordingly, Applicants assert that the claimed invention has both a specific and a well-established utility and respectfully request that this rejection under 35 USC 101 now be withdrawn.

Rejection under 35 USC 112, first paragraph

Claim 1, as presented on April 4, 2005, stands rejected under 35 USC 112, first paragraph. Specifically, the Examiner asserts that since the claimed invention is not supported by either a clear asserted utility or a well established utility, one skilled in the art would clearly not know how to use the claimed invention.

Applicants respectfully disagree with the Examiner's assertions.

It has been established by prior arguments in the instant response that the claimed invention has both a clear asserted utility and a well established utility. Applicants assert that one of skill in the art would know how to use the claimed biopolymer marker (amino acid residues 2-18 of SEQ ID NO:1) as a marker for Alzheimer's disease; therefore, Applicants respectfully request that this rejection under 35 USC 112, first paragraph now be withdrawn.

CONCLUSION

In light of the foregoing remarks and amendments to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,

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